



APPENDIX TO AMENDMENT AND RESPONSE

IN THE SPECIFICATION

On Page 14, please delete the 1st full paragraph beginning "The mutational patterns that have been observed and reported" and insert the following paragraph:

-- The mutational patterns that have been observed and reported for HIV-1 and that correlated with drug resistance are very diverse: some antiretroviral agents require only one single genetic change, while others require multiple mutations for resistance to appear. In HIV-1 there are currently approximately 100 mutations that are thought to be involved in the development of HIV-a therapeutic agent resistance. One such example is N88S, which causes *in vitro* hypersensitivity to amprenavir. See, e.g. Ziermann et al., *J. Virol.* 74(9):4414-9 (2000). A summary of mutations in the HIV genome correlated with drug resistance has been reported. Schinazi, R.F., Larder, B.A. & Meliors, J.W. 1997. *Int. Antiviral News.* 5, 129-142 (1997), herein incorporated by reference. Additionally, an electronic listing with mutations has also become available [at] on the internet at sites such as hiv-web.lanl.gov or www.viralresistance.com. - -

IN THE CLAIMS

Please amend claims 1, 13, and 20 as follows:

1. (Amended) A method for predicting resistance of a pathogen to a therapeutic agent comprising:

(a) providing a trained neural network that is trained using a training data set comprising members that correspond to at least one genetic

mutation that correlates to a phenotypic change that causes a change in resistance of the pathogen to the therapeutic agent;

(b) providing a determined genetic sequence from the pathogen; and

(c) predicting resistance of the pathogen to the therapeutic agent using the determined genetic sequence and the trained neural network to identify at least one mutation of the determined genetic sequence that confers resistance to the therapeutic agent.

13. (Amended) A method for predicting resistance of a pathogen to a therapeutic agent comprising:

(a) providing a neural network;

(b) training the neural network on a training data set, wherein each member of the training data set corresponds to a genetic mutation that correlates to a phenotypic change that causes a change in therapeutic agent resistance of the pathogen;

(c) providing a determined genetic sequence from the pathogen; and

(d) predicting resistance of the pathogen to the therapeutic agent using the determined genetic sequence and the trained neural network to identify at least one mutation of the determined genetic sequence that confers resistance to the therapeutic agent.

20. (Amended) A trained neural network capable of predicting resistance of a disease to a therapeutic agent, wherein the trained neural network comprises:

(a) a set of input nodes, wherein each member of the set of input nodes corresponds to a mutation in the genome of the disease; and

(b) a set of output nodes, wherein each member of the set of output nodes corresponds to the therapeutic agent used to treat the disease

and wherein the trained neural network was trained using a training data set comprising members that correspond to at least one genetic mutation that correlates to a phenotypic change that causes a change in resistance of the disease to the therapeutic agent;